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MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

FUNCTIONAL ASSESSMENT

OF

LASER IRRADIATION

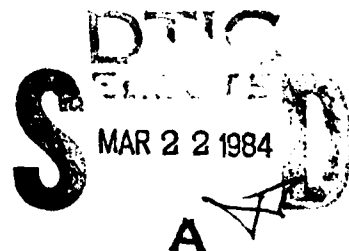ANNUAL PROGRESS REPORT 1981-82

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October 1981

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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Maximal visual acuity and normal color vision are closely associated with foveal receptor function. When the fovea is destroyed or altered by intense laser light, severe and often permanent losses in visual sensitivity ensue. In this report we have shown that the threshold for long-term functional alterations is determined not only by the wavelength and corneal exposure power of the laser flash but also by the types of performance criteria used to assess visual sensitivity. Effects of minimal diameter spots were also examined in one subject exposed to Argon light.

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INTRODUCTION

Light of sufficient power densities on the retina which elicit ophthalmologically visible lesions not only alter retinal morphology but also change the sensitivity of the observer to visual stimuli. The degree of degradation in visual sensitivity is dependent upon a number of factors, both in terms of the task used to assess visual activity and in terms of the parameters surrounding the light exposure. Depending upon the wavelength, duration and power density of the light, the induced structural damage may be the result of either thermal, mechanical or actinic insult. Associated with each of these different damage mechanisms may be different types of alterations in visual sensitivity. For example, if a relatively low energy exposure is short in duration and involves a significant portion of the fovea, both normal color vision and maximum visual acuity will be affected. The duration of the acquired deficit and the specific depressions in spectral sensitivity will depend on the power density and wavelength of the exposure. Longer duration exposures, regardless of its diameter, will produce more extensive damage throughout the retina in a non-anesthesized subject and will cause a greater shift in postexposure visual acuity and both photopic and scotopic spectral sensitivity.

Historically, the maximum permissible exposure (MPE) to laser light has been based primarily on morphological criteria. Morphological assessments have included gross fundoscopic examination of the eye following acute exposure to intense irradiation as well as more sophisticated examination of the cellular layers within isolated sections of the exposed retina. Generally, lesser power densities on the retina are needed to demonstrate ultrastructural changes within the retina by an electron microscopic technique than when only fundoscopic examinations are made. Both of these morphological techniques, however, have provided information as to the extent and site of the primary damage as well as the energy levels involved in producing such structural alterations. Traditionally, single exposures of relatively long durations involving large areas of the retina beyond the fovea have been employed to determine the MPE. While these exposure conditions may be necessary to facilitate visual verification of the induced structural alteration, they do not correspond well to the type of condition under which accidental exposures may occur in the field. Two different types of hazards will typically exist with the increased employment of lasers in the field. The first is either accidental or intentional exposure to an intense but brief laser beam, the source of which would presumably be some distance away. Associated with this type of exposure would be structural alterations in relatively isolated areas of the retina. Depending upon the situation surrounding the exposure, ultrastructural alterations may be either in the fovea or periphery. The second type of exposure is the intentional viewing of presumably safe and low level diffuse irradiation over relatively long time periods; days, weeks, or

even months. Such exposure, if hazardous, will generally cause damage throughout the retina and produce a more gradual shift in visual sensitivity than will higher energy, point source exposures of an acute nature.

While these morphological data have greatly contributed in the development of the ANSI guideline, they provide no data regarding the degradation in visual performance following exposure near to or above the MPE. Such information is critical when discussing the possibility of completing a visually-guided mission by a person exposed to an intense, short duration laser flash. Further, morphological criteria alone may not be the most sensitive criteria for determining MPE. Minute enzyme and cyclic biochemical changes in the photoreceptor and associated structures may occur at levels where immediate morphological damage is not readily apparent. Such actinic insult may, however, adversely affect the overall functioning of the photoreceptor and thus produce changes in the electrophysiological response of the retina as well as its sensitivity to light.

In most behavioral studies, like morphological studies, anesthesia has been required for the placement of the exposure onto relatively small and predetermined areas of the retina. An exception are those behavioral studies where the subject is chronically exposed to diffuse laser light. In these cases ultrastructural alterations are usually spread throughout the retina and not isolated to foveal areas which makes individual examination of each alteration behaviorally impossible. If specific retinal areas are to be acutely irradiated with small diameter spots, then the animal must be immobilized with anesthesia, thereby eliminating all possibilities of immediate postexposure behavioral testing. The lack of information regarding the animal's visual sensitivity for the first 24 hours or more following exposure seriously limits the exploration of transient changes in acuity and allows for the examination of only those effects which are relatively severe and long lasting. The immediate changes in visual performance are critical in determining how personnel will be able to function within their mission once exposed. In addition, these immediate alterations are important both in the exploration of minimal thresholds as well as testing for any cumulative effects repeated exposures may have in determining the MPE. In the initial phases of this contractual effort, a behavioral procedure was designed and implemented which produces consistent foveal exposures in awake, task-oriented animals. This procedure, along with a modification of a rapid technique to measure rhesus visual acuity, has been used in the current support period to assess the immediate behavioral consequences of brief exposures to laser light both above and below those power densities which produce long term effects.

In previous protocols, the behavioral effects of variations in the diameter of the spot on the retina and its wavelength were examined in several animals. The rationale for the use of larger spot sizes (>300 microns) was to make the results of these functional explorations more compatible with morphological and electrophysiological studies underway in other research laboratories

which have traditionally used larger diameter exposures. Larger
diameter exposures obviously facilitate histological identifica-
tion of retinal alterations and allows for our animals also to be
examined histopathologically following their completion of the
behavioral portion of this project. Another advantage of larger
spot sizes is that they increase the probability of a foveal ex-
posure in any given exposure session and elicit larger shifts in
visual acuity following a successful exposure. These advantages,
however, are largely procedural and do not necessarily imply that
larger diameter spots are more appropriate than smaller ones to
determine the MPE. In fact, the opposite may be true. The ra-
tionale for the use of smaller spot sizes was to be more closely
simulate the type of exposure condition which might occur in the
field from which personnel must be protected. In all of our pre-
vious studies even our smaller diameter spots were relatively
large in comparison to a distant point source which might be en-
countered in the field. During the current phase of this project
we have been exposing animals to even smaller diameter spots
(<50 microns) and have been measuring the consequences such ir-
radiation has on visual sensitivity.

Variations in the exposure wavelength have also been examined.
Such variations are important when attempting to generalize the re-
sults of our behavioral studies to as many different laser sources
as possible. Exposure wavelength has been shown by our studies to
be an important variable in determining the MPE for lasers. Func-
tional thresholds as well as the type of shift in chromatic sen-
sitivity following exposure has been shown to be dependent upon the
wavelength of the exposing source. Also, the examination of
specific wavelengths has helped in delineating the nature of the
damage mechanism. At the present time we have examined the effects
of three different spectral lines: 632.8 nm (HeNe), 647.1 nm
(Krypton) and 514.5 nm (Argon).

In our previous behavioral studies, the immediate as well as
long term effects of laser irradiation on visual sensitivity have
been measured using a Landolt ring discrimination task. The advan-
tage of the Landolt ring over grating targets is that the break in
the ring relates more specifically to small and more defined re-
tinal regions. Acuity has been measured using both achromatic and
chromatic background targets. In the current support period we
have expanded the use of chromatic targets during and immediately
following exposure. These chromatic tasks are more appropriate in
assessing changes in foveal sensitivity than are achromatic ones
since it is the fovea where color vision predominates. We have
also begun examining what effects different contrast targets, both
chromatic and achromatic, have on determining postexposure sensi-
tivity and the MPE. The use of lower contrast targets than those
previously used in this study will more accurately simulate field
conditions and hence will more precisely determine the ability of
exposed personnel to complete visually-guided missions.

In the current support period we have measured the immediate
as well as long term recovery of visual acuity following brief

exposures to Argon light. The long term consequences of repeated
low level exposures were also examined and compared to similar ex-
posures to HeNe and Krypton laser light. Initial exposures were
presented well below the MPE and the power density of the exposure
was then systematically increased in discrete steps over a period
of several months until the recovery process was no longer com-
plete within a single test session. Following stablization of new
baseline levels below those determined during the pre-exposure
testing, or following a return to the pre-exposure level at some
later date, the animal was re-exposed and recovery again plotted.
All recovery functions were derived using a continuous assessment
of the subject's postexposure sensitivity. Postexposure examina-
tion of any visual deficit consisted of a number of different vis-
ual tasks including: spectral sensitivity, contrast sensitivity,
and spectral acuity. The goal of this project has been to deter-
mine the MPE for various laser sources using a behavioral analysis,
and then to extrapolate both the threshold power densities and
the magnitude of elicted deficits in visual sensitivity from our
rhesus model to the human. The hypothesis is that receptor via-
bility and recovery for the rhesus and human are similar and the
energ   necessary to elicit such effects are only displaced along
a continuum due to differential pigmentation and retinal illumi-
nation for the same external light source.

Methods

In previous reports and papers we have presented a method to
expose awake, task-oriented rhesus monkeys (Robbins, Zwick, &
Holst, 1974); a procedure necessary to record immediate changes in
acuity following exposure. Visual acuity was measured using con-
ventional black Landolt rings against achromatic (white) or chro-
matic backgrounds. Rhesus were trained to press a lever whenever
a Landolt C was presented and not to respond when gapless rings
were presented. If the subject failed to respond to a Landolt C
during the 2 sec presentations, or if he responded to a gapless
ring, he received a brief electric shock which was annoying but
not highly painful or dangerous. Landolt C's were randomly ar-
ranged within a series of equally-sized, gapless rings. All test
targets were projected onto a rear projection screen by a stand-
ard carousel projector. A second projector served as a diffuse
source of light when different contrast levels were presented.
Threshold acuity measurements were obtained by a tracking method
which allowed the subject to adjust the size of the test object
about his threshold. All testing was performed monocularly under
photopic conditions. Chromatic backgrounds were equated for equal
numbers of quanta.

A diagram of the optical system is presented in Figure 1. A
4 W Argon laser served as the light source. The diameter of the
beam on the retina was varied from greater than 300 microns when
the expanding telescope and collimating lens were in the optical
pathway to less than 50 microns when the lens assembly was removed.
The power density of the laser beam was controlled by the laser

source itself and by neutral density filters placed in the optical pathway. The beam was aligned such that it was coaxial with a line between an artificial pupil and the gap in a specified Landolt ring subtending less than 1 min of arc. The beam passed through a converging lens positioned such that the cornea was in the focal plane of the lens. When the animal was properly positioned, the beam entered the eye through the gap in a threshold Landolt ring which exposed the fovea; the area of the retina the animal was using to fixate on the critical feature of the discriminable target. All exposure durations and power densities were measured.

To assure proper orientation of the animal toward the screen, the animal's head was rigidly held in a fixed position during all behavioral testing. The animal was also fitted with an opaque
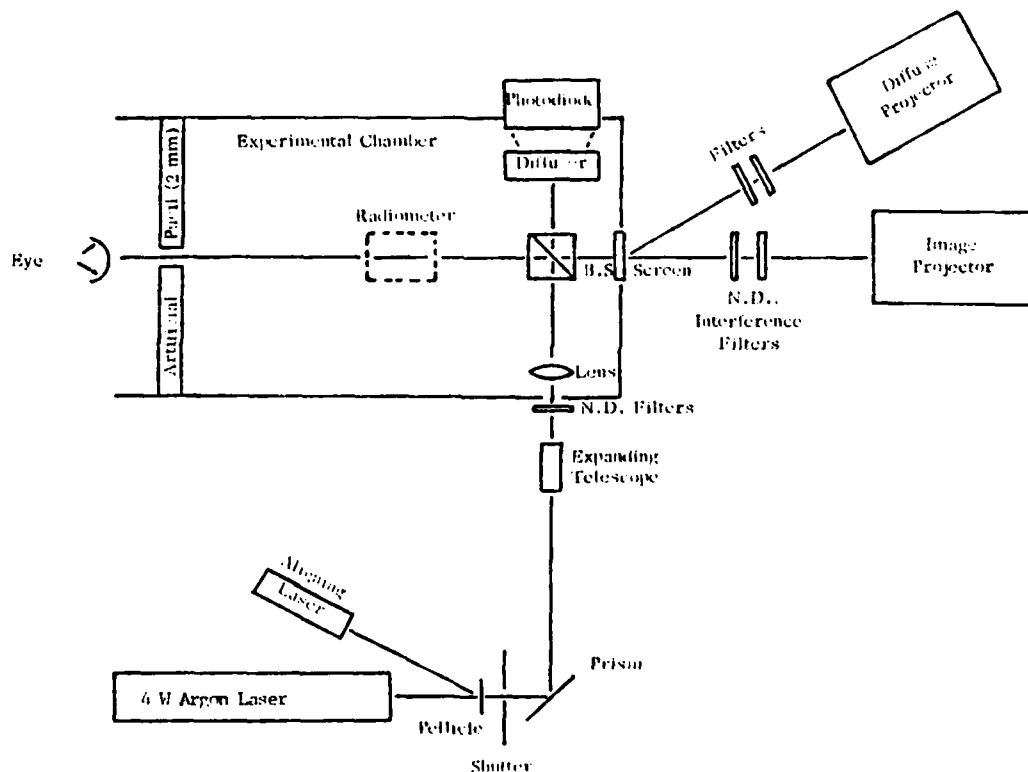

Figure 1. Optical system

facemask and monocular iris diaphram. These restraints minimized the effects of small pupillary changes and lateral head or eye movements during testing since any voluntary movements of any sort would block the animal's line of sight to the screen and result in the animal being shocked from incorrect detections. These procedures resulted in a high probability (in excess of 75%) that laser irradiation, regardless of its diameter on the retina, would produce a significant shift in maximum visual acuity. Shifts of the nature observed would imply foveal involvement since peripheral involvement only would not have produced any shift in maximum photopic acuity.

All exposures were of 100 msec duration. Such relatively short exposure durations were necessary to eliminate voluntary and involuntary eye movements away from the light. Exposures were triggered by the animal's correct detection of his threshold Landolt ring. Exposures were made over power levels from 0.3 mW to 3 mW measured at the cornea, beginning with the lowest power level. No more than one exposure was made per day and each power level was repeated a minimum of 4 times for each exposure condition. Exposures were made while the subject was viewing one of four different chromatic backgrounds at one of three different contrast levels. Immediately after exposure the recovery of acuity was measured using achromatic and chromatic targets. If the subject failed to return to his pre-exposure acuity within the 2 hr session, further exposures on subsequent days were suspended and daily baseline measures of spectral and white light acuity were obtained

Results

Sample data of threshold acuity using the tracking technique is shown in Figure 2. In this particular session the subject was exposed to a 7 mW, 150 micron HeNe flash of 100 msec duration. The occurrence of the exposure is indicated in the figure by an arrow (also the zero point on the abscissa). The ordinate indicates the various sizes of gaps in presented Landolt rings and is plotted in reciprocal minutes of arc. Horizontal excursions of the chart represent the presentation of these targets. The abscissa represents corresponding times (in minutes) for representative Landolt C trials relative to exposure. Each Landolt C target was randomly positioned into a series of equal-sized, gapless rings. The presentation of the gapless rings is indicated on the chart by vertical excursions between the horizontal excursions. The order of presentation of the slides in terms of their diameter (and hence acuity) was entirely dependent upon the animal's response on Landolt C trials. Incorrect detection of the Landolt C caused the recorder to plot downward and corresponded to the presentation of larger diameter rings.
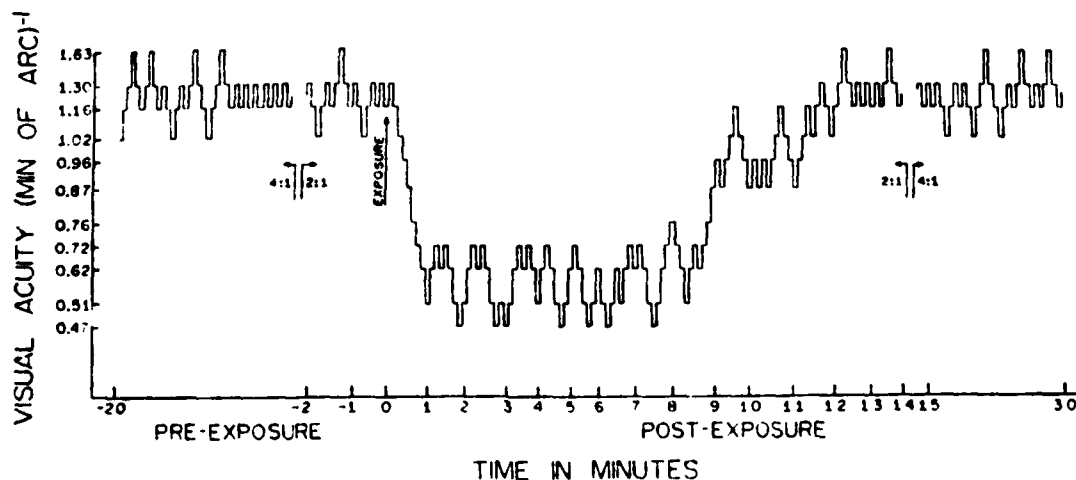

Figure 2.   Raw data recovery function.

Prior to exposure, the animal's mean acuity under maximum photopic conditions was 1.25 (min of arc)$^{-1}$. Immediately following exposure the animal's acuity to achromatic targets decreased to 59% of its pre-exposure level which represented an acuity level of 0.51 (min of arc)$^{-1}$. Following an initial stablized depression of nearly eight minutes, the animal's sensitivity gradually returned to its pre-exposure level in approximately 13 minutes. The magnitude of the initial deficit in visual acuity following exposure was found to be independent of exposure power. With a larger retinal spot size of 323 microns, however, significantly larger initial deficits (69% to 86% of pre-exposure levels) were produced representing an inactivation of a larger portion of the retinal mosaic. In preliminary exposures with minimal diameter spots (<50 microns) the size of the initial deficit was not significantly less than that produced by a 150 micron spot. The magnitude of the initial deficit as well as the length of time for full recovery was also dependent upon the type of target used to track visual sensitivity. With chromatic targets the initial deficit in acuity varied from 0.4 (min of arc)$^{-1}$ for backgrounds of 560 nm to 0.20 (min of arc)$^{-1}$ for backgrounds of either 640 or 480 nm for Krypton exposures. Argon exposures produced slightly different maximum deficits, but for each of the laser sources, the magnitudes of these deficits for any specific wavelength target was independent of the energy of the flash. The contrast level of the target also affected the time necessary for full recovery independent of exposure energy.

Long term deficits in spectral sensitivity were produced in one animal following repeative 3.0 mW laser exposures (see Figure 3). The diameter of the exposure on the retina was 323 microns and single exposures of 100 msec duration were separated from one another by at least 24 hours. These spectral sensitivity curves were derived beginning four months following the last 3.0 mW exposure. The solid line in each figure represents the spectral sensitivity of the exposed eye while the dashed line represents the sensitivity of the unexposed eye. A Landolt ring acuity task was used to derive these curves and three different criterion curves are shown. These different criterion curves were calculated from intensity-acuity functions at various spectral points across the visible spectrum. No significant difference existed between the sensitivity of the control (unexposed) eye pre- and postexposure or between the postexposure control eye sensitivity and the pre-exposure sensitivity of the exposed eye. For all criteria shown, sensitivity was depressed most to the very long (beyond 600 nm) and very short (below 460 nm) wavelengths. Sensitivity was also greatly reduced in the region of the spectrum near the wavelength (514.5 nm) of the exposure source. Standard deviations for each of the spectral points have been calculated for both within and between sessions. These measures of variability were excluded for reasons of clarity but do show, along with appropriate statistical tests, that the differences between these exposed and unexposed eyes in the spectral regions mentioned above were statistically significant. We have continued to follow this animal's spectral sensitivity and with time there has been a slight recovery in sensitivity of the exposed eye especially in the very long and short
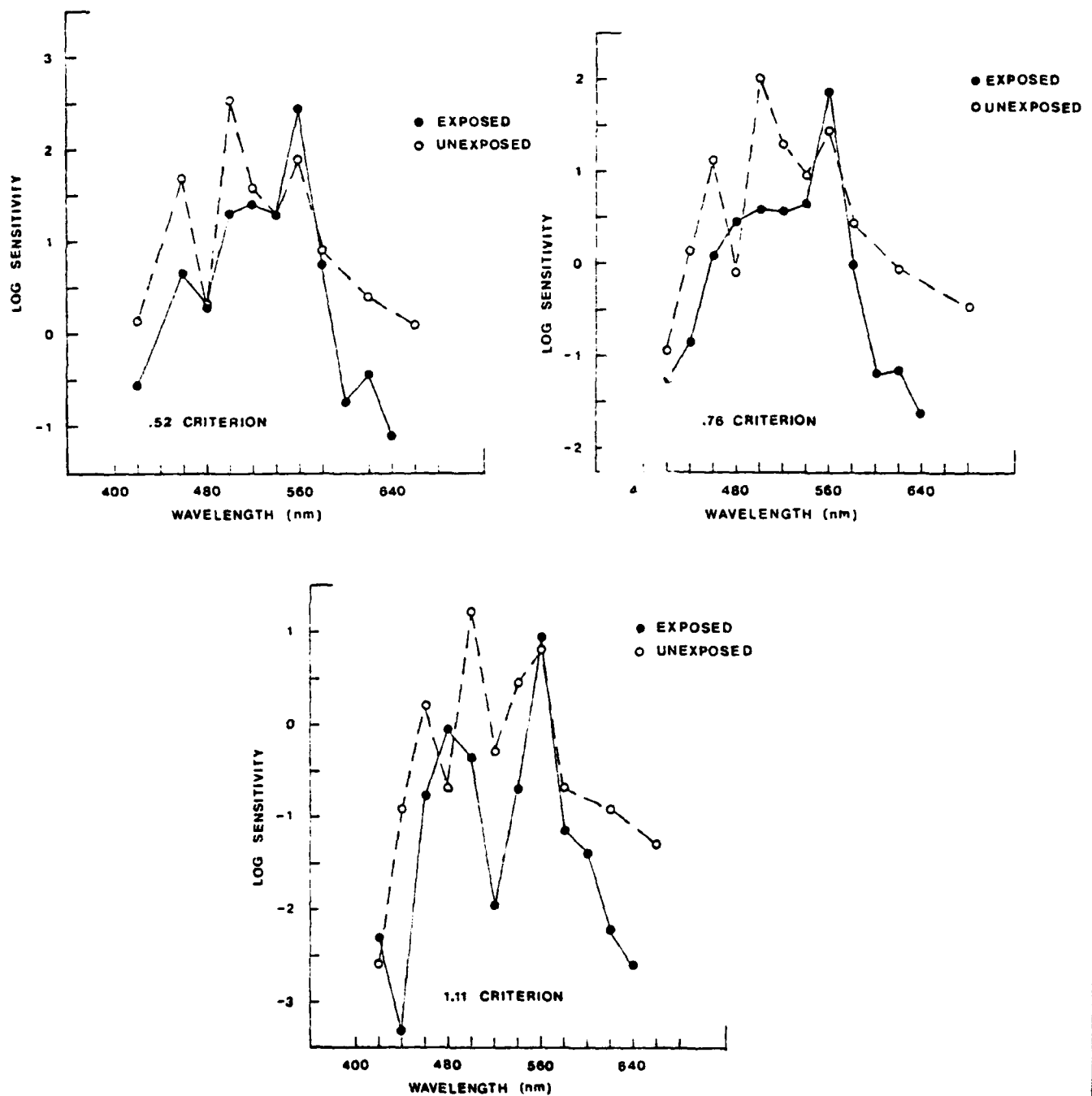
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Figure 3. Spectral sensitivity curves for one animal exposed to an Argon laser.

regions of the visible spectrum. Nearly six months later, there are no significant differences between the sensitivities of the two eyes although the exposed eye generally remains depressed in the same regions of the spectrum as shown in this figure.

Visual acuity, measured under four different contrast levels, is shown in Figure 4 for the same animal as shown in Figure 3. The upper curves represent the acuity of this animal's exposed and un- exposed eye to dark Landolt rings projected onto white backgrounds. Acuity was tracked or titrated, in terms of gap size, in the manner described previously. These achromatic contrast curves were derived three months after this animal was exposed to laser irradiation of sufficient power density on the retina to produce a long-term, significant shift in visual performance. The original indicator of visual performance was visual acuity measured for various chro- matic background targets under maximum photopic, contrast conditions. Tests to determine the significance of the differences between the exposed and unexposed eye (T-test/ANOVA) were significant at the 0.05 level for all contrast conditions. Similar functions were derived for several different chromatic backgrounds and their differences were likewise significant. Four months later, recovery in visual sensitivity was nearly complete and little or no differences existed in terms of contrast sensitivity or spectral sensitivity be- tween the exposed and unexposed eye. In the lower portion of Figure 4, acuity for four different contrast levels is shown using chro- matic, 620 nm backgrounds. These measures were made during the later stages of the recovery process and demonstrate little differences between the two eyes. No measures made in recent weeks indicate any residual deficit in this animal even though nearly three months earlier, this animal demonstrated large, long-term deficits in a number of measures of sensitivity in the exposed eye. This animal is again being exposed to Argon irradiation and immediate recovery functions examined under a wider range of test parameters then previously used. In all subsequent exposures to date, the animal has shown no long term deficit following exposure to power densities at and below that which produced the first long-term deficit.

Animals exposed to laser flashes not intense enough to pro- duce permanent shifts in sensitivity, demonstrate that the duration of the initial recovery process is influenced by the contrast level of the targets used to assess this process. In Figure 5, three different recovery functions are shown for one animal exposed to three similar 3.0 mW, 323 micron, Argon flashes spaced at least three days apart. Immediate postexposure recovery is plotted in percent deficit in visual acuity from the animal's pre-exposure acuity level as a function of time following exposure. In the upper portion of this figure is shown a condition under which optimal contrast (97%) existed between the dark Landolt ring and the back- ground. Recovery in this case was complete within the first 25 minutes of exposure and no long term deficit existed 24 hours post- exposure. Using the same exposure conditions but lower contrast between the target and background (60%), full recovery occurred after a longer period but was completed within the 40 minute post- exposure test session. With a minimal contrast target (40%) similar
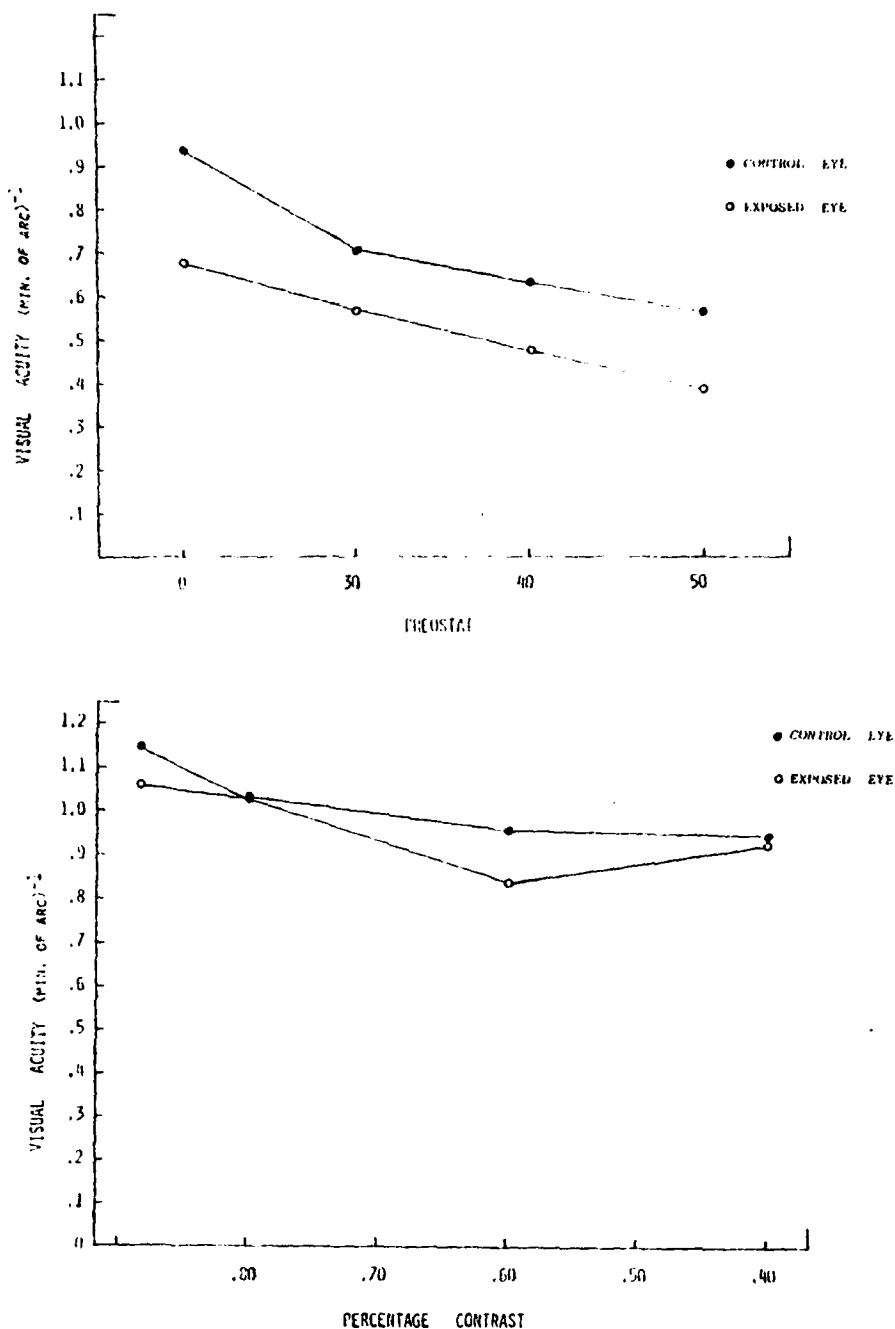
Figure 4.   Effects of contrast on visual acuity in an exposed
animal.

exposures produced deficits which were not complete within the
immediate postexposure session even though 24 hours later no sig-
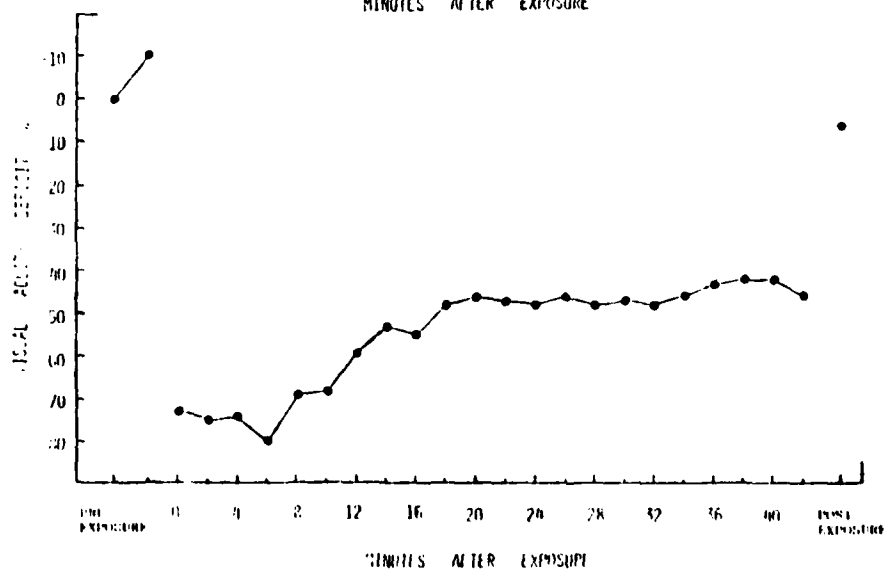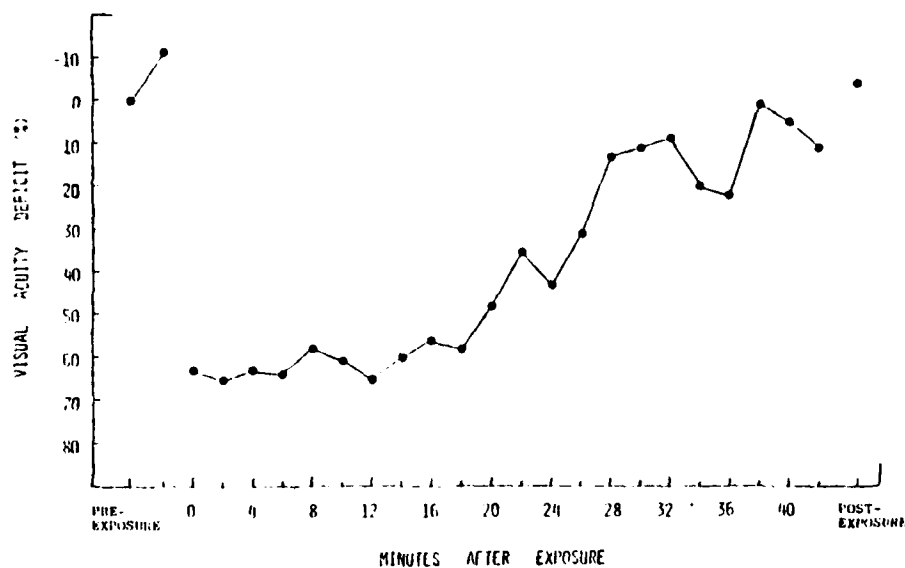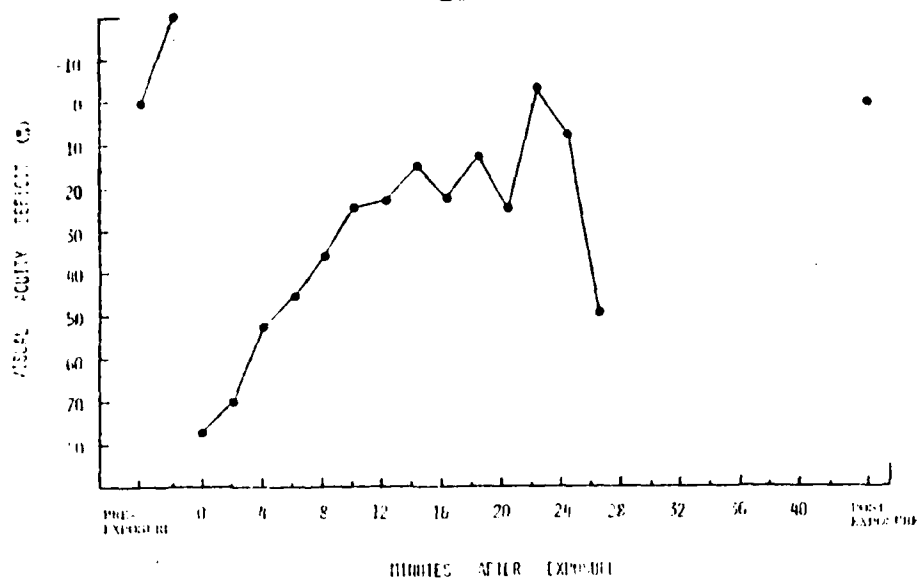nificant deficit was evident using this type of testing condition.

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Figure 5.   Effects of contrast on the time course of the recovery
process.

These differences in the observed recovery process were not the result of differences in the adverse effects of the separate laser exposures, but rather the result of the behavioral instrument used to assess these adverse effects. Switching the contrast level of the viewing target during the initial stages of the recovery process altered the level of deficit in relation to the animal's pre-exposure baselines.

Preliminary examination of the behavioral effects of minimal diameter spots (<50 microns) on the retina have shown inconsistent results. In Figure 6, for example, the immediate recovery functions of one animal to three separate, but similar, exposures are shown. In all three exposures visual performance was measured using medium contrast (60%), 620 nm targets. In the top curve, the animal is shown to return to his pre-exposure acuity level quite rapidly. This recovery is less rapid than that which would have been expected if no exposure had occurred (control condition) or if peripheral, rather than central, areas were the site of the actual retinal exposure. In either of these latter cases the carousal would have immediately begun tracking backward following its manual readjustment and would have returned to its original level in approximately 3 min. Instead, it took approximately 10 min. before the projector reached the level at which it was prior to exposure. This longer time period was the result of the animal's incorrect detections of targets above his pre-exposure threshold during the first several minutes of postexposure testing which caused the projector to reverse directions several times before returning to its pre-exposure position. This recovery time, however, was more rapid than those observed with 323 micron spots of equal duration and energy (see Figure 5, middle function) or those observed during other similar minimal spot exposures as indicated in the bottom two functions in Figure 6. In all of these examples, the same measure of visual performance was used. The longest duration for recovery shown in the bottom graph was not due to any cumulative or residual reaction to repeated stimulation since it actually occurred three days prior to the one shown in the middle graph.

Discussion

Permanent functional alterations associated with laser exposures have been produced at corneal irradiances below those previously reported using gross fundoscopic or fine histological criteria. Further, the effects of low-level irradiation appear selective depending upon the energy, diameter, and wavelength of the exposing source as well as upon the number of previous exposures made. In addition, the type of tasks used to assess visual performance will greatly affect the magnitude and time course of any charted recovery process. In comparison to previous exposures with other wavelength laser sources, the threshold for permanent function-
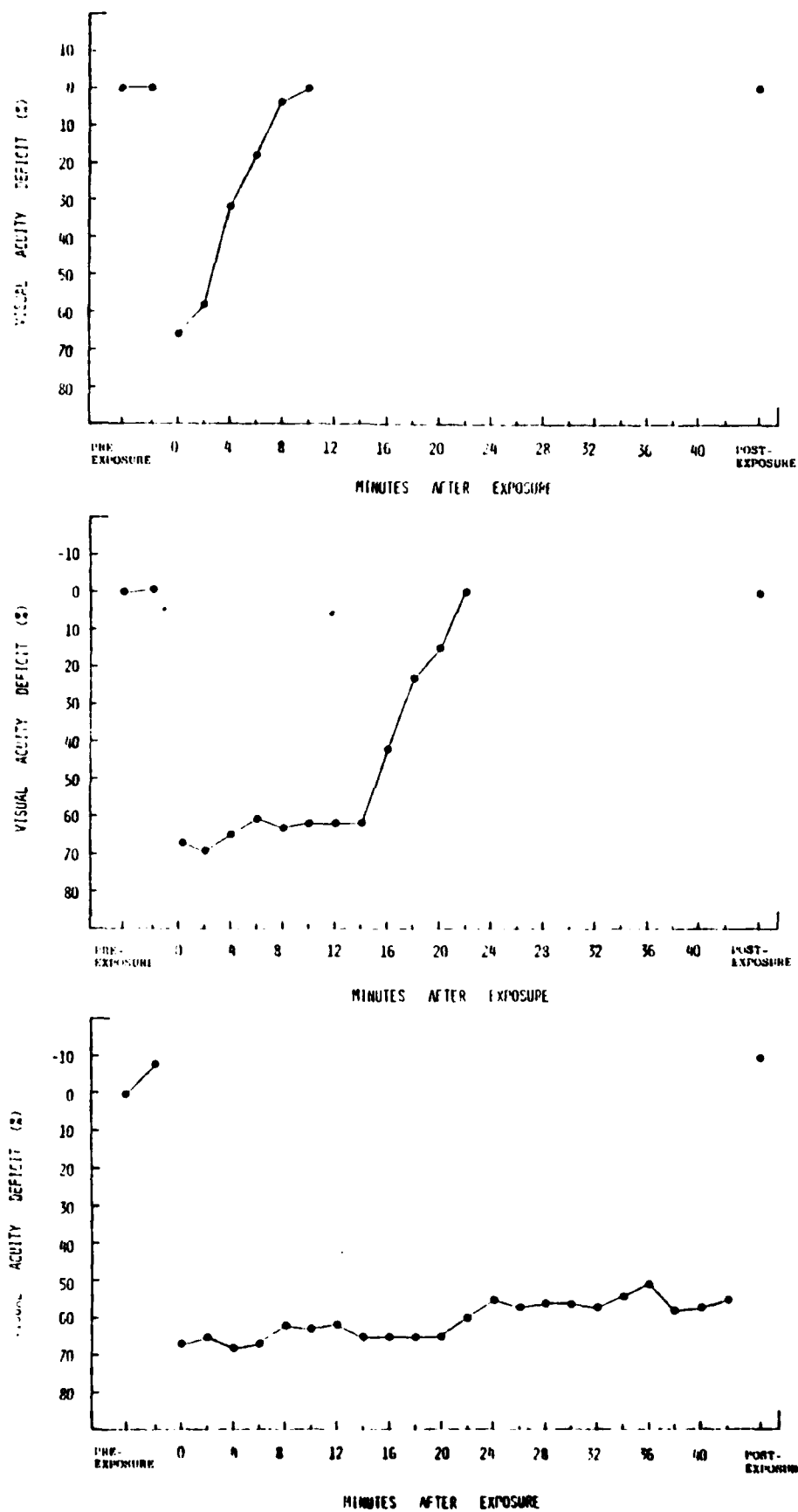
Figure 6.   Repeated 3.0 mW exposures using a minimal spot.

al alterations in chromatic acuity was lower for Argon irradiation than for either HeNe or Krypton irradiation. Our data suggest that specific spectral lines of coherent light at low levels selectively alter specific foveal cone processes and the use of acuity targets of different colors and contrast best delineate this effect.

In all of our studies, the transition from temporary to permanent losses in visual acuity occurred after a succession of exposures at the same corneal irradiances and not after the first exposure at any particular exposure level. This phenomenon occurred in spite of the fact that we waited a minimum of 24 hours between repeated exposures and longer if the animal had not fully recovered within the original 2 hour test session. Such an effect is strongly suggestive of some cumulative process occurring in the eye to repeated exposures. A similar result was shown when animals were exposed to daily low-level, diffuse Argon irradiation using a slightly different behavioral paradigm (Zwick, Bedell, and Bloom, 1974). These results are more closely analogous to reported temporary and permanent threshold shifts in audition than those reported for the visual system. No distinct long-term chemical process has yet been implicated within the eye in which changes of this nature and time course could be explained. Other equally acceptable explanations could include changes in receptor or neural electro-chemical activity or structural changes either in the receptor cell, pigment epithelial cell or other accessory structures associated with light reception and transmission.

Several important conclusions can be drawn from our studies thus far which need further examination and delineation in future contract efforts. First, the effects of intense, single-pulsed, laser irradiation appear cumulative. The time course and degree of additivity remain unknown, but nevertheless is an important consideration in any determination of safety standards. Second, monochromatic test targets appear to be a more sensitive measure of postexposure acuity than achromatic targets, especially for longer-wavelength laser exposures (HeNe and Krypton). Using Argon irradiation, both achromatic and chromatic acuity demonstrated a significant depression following relatively low level (3.0 mW) exposures, although acuity to chromatic targets remained depressed longer than acuity to achromatic background targets.

Third, the power density where a permanent functional alteration was found appears to differ significantly depending upon the wavelength of the exposing source (6.0 mW for Krypton and 3.0 mW for Argon). Compounding this conclusion, however, is any cumulative nature of the damage mechanism; although, with both exposing lasers, animals were exposed on an almost identical daily basis to similar increasing power densities on the retina. Fourth, low contrast visual acuity is more affected by laser irradation than is higher contrast acuity, and the use of these lower contrast acuity tasks may produce results more comparable to the types of visual

disruptions to be expected in field-related exposures. Lastly, the diameter of the exposure on the retina appears to affect the magnitude of the initial deficit for diameters which cover the central most fovea and beyond. For smaller diameter exposures (<50 microns), larger than predicted initial deficits are observed and the duration for full recovery becomes erratic.

These experiments have shown that functional analyses of the adverse effects of laser irradiation are a more sensitive measure than are either the morphological or electrophysiological approach. Further, they suggest that such analyses may be very important when one is determining safety criteria for high intensity light sources. This behavioral approach provides information not only for determining the MPE but also provides information regarding the nature of the change in visual sensitivity to be expected from any exposure. These experiments do raise questions as to the exact nature of the damage mechanism. No experiment or series of experiments, however, can include all of the necessary parameters to cover the possible questions which arise in the course of experimentation. Rather a series of key stimulus dimensions are being used to depict the underlying neurological and morphological mechanisms which alter visual performance and could disrupt successful completion of visually-guided missions. It is from the data of experiments such as these that we shall propose modifications in the existing safety standards or in the establishment of new standards where none now exist as in the case of chronic or repeative exposures. As this and other projects have shown, the sole use of a fundoscopic criteria, or for that matter any other single criterion, for assessing the deleterious effects of laser irradiation is inadequate in producing standards which will adequately protect personnel in the field. What is needed for the establishment of realistic standards is the correlation of data from many different approaches, each with its own unique assessment sensitivities to the damage process. It is nevertheless obvious from these studies that more investigations of this important environmental hazard is necessary and that modifications in the MPE should be made.

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